GLYCOSYLATED HAEMOGLOBIN AND FRUCTOSAMINE CONCENTRATION IN SOME VASCULAR COMPLICATIONS OF DIABETES MELLITUS

Thesis

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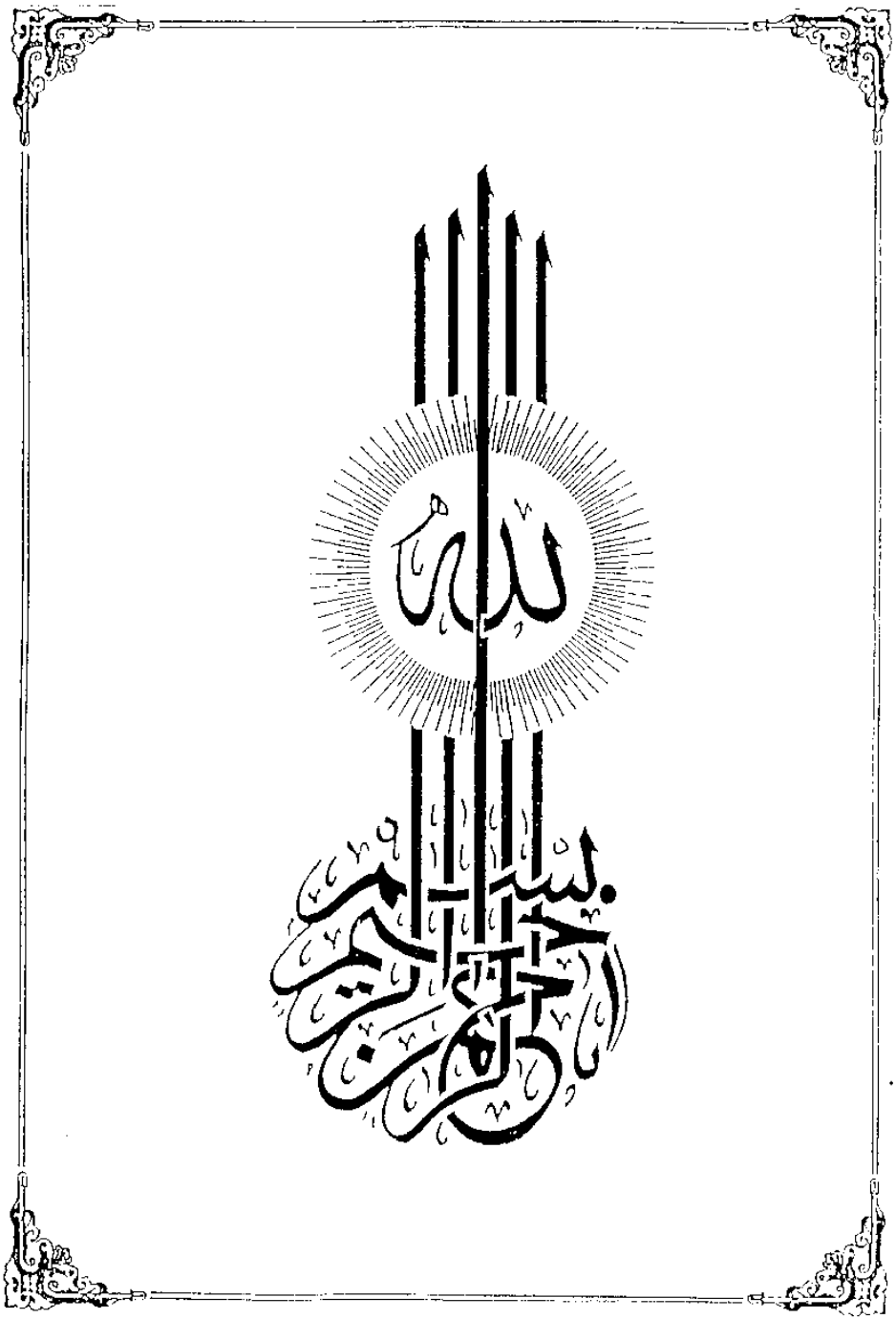
بسم الله الرحمن الرحيم

"وأنزل الله عليك الكتب والحكمة

وعلمك ما لم تكن تعلم وكان فضل

الله عليك عظيما"

صدق الله العظيم (النساء ١١٣)



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Introduction and AIM OF THE WORK

INTRODUCTION AND AIM OF THE WORK

Diabetes mellitus is a universal health problem occurs at any age, characterised by a state of chronic hyperglycaemia with a series of hormone-induced metabolic abnormalities and long-term complications involving the eyes, kidneys, B.V. and nerves.

The biochemical measurements for initially detected patients wiht diabetes mellitus are estimations of blood and urine glucose concentration. Although these tests are the commonly used methods, yet they are non-specific, being influenced by a wide variety of conditions and drugs. Moreover, blood glucose control is difficult to assess in patients with unstable type I diabetes mellitus, in whom the glucose concentration flactuate widely during the day and multiple daily blood glucose estimations are necessary to assess the glycaemic state accurately.

Recently other methods have been developed to measure glucose tolerance via estimating the concentration of the glycosylated Hb (G-Hb) and the concentration of the glycosylated serum proteins (fructosamine).

The estimation of the concentration of G-Hb in the blood of diabetic patients become widely accepted as the best index of the degree of glycaemic control in the preceeding 8-10 weeks **(Bunn et al., 1976)**.

The disadvantages of G-Hb estimation are, the technical difficulty and its long half life (6090 days), therefore reduction may not be apparent for weeks after the establishment of control **(Kennedy and Merimee, 1981)**.

Recently a new colorimetric method designed to measure serum glycosylated protein concentration called the fructosamine test. It is simple, rapid, accurate and it is not affected by the time of day or previous food intake **(Schleicher et al., 1983)**.

Day et al. (1980) stated that fructosamine test is the best index of the changes in blood glucose control during the previous 1-2 weeks.

The aim of the present work is to study the changes in G-Hb and fructosamine levels in diabetic patients with and without vascular complications and to use these concentrations as a marker in diagnosis of border line and high risk complications.

Review of Literature

VASCULAR COMPLICATIONS OF DIABETES MELLITUS

DIABETIC ANGIOPATHY

Deaths from acute metabolic complications have markedly decreased with the introduction of insulin therapy. The subsequent increased longevity of diabetics attributed to the occurence of vascular complications which have accounted for the majority of morbidity and mortality in diabetic patients **(Marble, 1976).**

According to morphological and pathological features, diabetic angiopathy is divided into two groups: diabetic macroangiopathy and microangiopathy **(Zetter, 1981).**

DIABETIC MACROANGIOPATHY

Atherosclerosis is the most common complication of diabetes **(Ganda, 1980).** Atherosclerosis of the major vessels of the lower limb is more common and more peripheral in its distribution than in non diabetic subjects **(Delbridge et al., 1985).** Atherosclerosis in diabetics appear at earlier age and with greater severity than in non diabetic population **(Ganda, 1980).** The disease

is more common in men with I.D.D.M. than in non diabetic men, but no difference is found in its prevalence between diabetic and non diabetic females **(Siitaneno et al., 1986).**

Diabetic atherosclerosis expresses itself as ischemic heart disease, cerebral strokes, intermittent claudication and gangrene of lower limbs **(Bradley, 1971). Garcia et al. (1974),** stated that myocardial infarction is up to four times more common is diabetics than in non diabetics. While **Jones et al. (1981)** said that the coronary heart disease and cerebral strokes are twice that of the non diabetic population.

Diabetes show evidence of a state of hypercoagulability **(Ganda, 1980),** this hypercoagulability is related to changes in platelets, R.B.Cs. and fibrinogen **(Delbridge et al., 1985).** Several factors suggest a role of hyperglycemia in development of tissue hypoxia which could be a significant factor in atherogenesis **(Ganda, 1980).**

The role of impaired lipid metabolism were studied by many investigators. **Sosenko et al. (1980),** suggested that the vascular effects of diabetes were the result of formation of altered plasma lipids (dyslipoproteins). **Wolinsky and associates (1978)** noticed that the specific activity of enzyme cholesterol ester hydrolase, was decreased in diabetes, this favours accumulation of cholesterol in the arterial wall.

Recent studies suggest that the platelets and prostaglandins play an important role in the development of atherosclerosis in diabetes. **Halushka et al. (1977),** stated that there was abnormality in the prostaglandins metabolism in the platelets and endothelium in diabetic patients, together with increased levels of circulating prostaglandin E. Moreover, **Lufkin et al. (1979)** described activation of platelets with increase their adhesiveness in both types of diabetes IDDM and NIDDM prior to the development of clinically apparent atherosclerosis. Other factors responsible for the development of atherosclerosis in diabetes are endothelial injury, smooth muscle proliferation and interaction between the platelets and arterial wall which enhanced by prostaglandins **(Fuster and Chesebro, (1982).**

On other hand **Moncada and Vane, (1978)**, stated that platelets adhering to sites of vascular damage in diabetes release a sepcific substance-thromboxane A_2-which promote further aggregation of platelets at these sites.

DIABETIC MICROANGIOPATHY

Arteriolar and capillary diseases are much more extensive in diabetic than in non diabetics subjects. Diabetic angiopathy is characterised by thickening of basement membrane of small vessels and capillaries in the retina, kidney, myocardium and vasa nervosa. The thickening of the vessel walls are due to deposition of homogenous or granular hyaline material that start in the intima and later on replace the media. Diabetic microangiopathy may be attributed to the raised levels of circulating immune complex which originate secondary to the wide spread tissue damage in diabetes of long duration **(Bodansky, 1982)**.

Kloppel, (1985); stated that diabetic microangiopathy is characterised by thickening of basement membrane and microaneurysms of small blood vessels. Moreover, **Williamson**

and Kilo, (1977); discovered that the microangiopathy was closely related to the degree and duration of hyperglycaemia.

Electron microscopic studies were done on the renal glomeruli by **Steffes et al. (1979) and Kilo et al. (1972),** showed an increase in the glycoprotein basement membrane after the onset of diabetes and progress with the duration of the disease.

The exact biochemical relation between sustained hyperglycemia, basement membrane thickening and disturbed function is not yet known, but **Spiro, (1976);** suggested that increase glycosylation of the protein induces diabetic microangiopathy.

In addition to protein glycosylation, platelet abnormality may contribute to diabetic microangiopathy. Significant platelet microthrombi have been observed in diabetic microangiopathy **(Bloodwoorth and Molitor, 1965).**

Pathogenitically, it is still uncertain how does diabetes predispose to all these vascular lesions. The more important postulates are metabolic **(Westberg, 1976; Paving and Mogensen, 1976)**, genetic **(Marble et al., 1973)** and autoimmune reaction to insulin **(MacLeod, 1981)**. The metabolic aspect will be dealt with later but reference here may be made to the finding that the thickened basement membrane is due to deposition of a glycoprotein containing approximately 20% of carbohydrate **(Spiro, 1976)**. Lipid deposition could also be demonstrated. Both the P.A.S. thickening and lipid deposition result from insudation of plasma constituents through an abnormally permeable endothelial lining **(Ashton, 1974)**.

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